regimens vary and may affect treatment outcomes. In this retrospective analysis, we investigated if IV busulfan dosing (total dose 3.2 mg/kg vs. 6.4 mg/kg) in fludarabine/busulfan (Flu/Bu) RIC regimens would affect outcomes in patients undergoing HCT for MDS or AML. A total of 217 patients with MDS or AML underwent Flu/Bu RIC PBSCT from well matched related or unrelated donors at our institutions between 2004 and 2009. 135 patients received Bu1 (busulfan 0.8 mg/kg/d x 4 while 82 patients received Bu2 (busulfan 0.8 mg/kg bid x 4), both with daily fludarabine (30 mg/m^2/d x 4 days). The choice of RIC regimens was based on temporal institutional standard, enrollment on protocols, and physician choice. Patients had similar characteristics with a few notable differences: patients receiving Bu1 were younger (median age 61 vs 64, $p<0.001$), received more single-antigen mismatched unrelated grafts (14.1% vs. 1.2%, $p<0.001$), received more sirolimus based GVHD prophylaxis regimens (63% vs 45%, $p < .0001$), received less ATG for GVHD prophylaxis (0% vs. 22%, $p < 0.001$) and had less enrollment on a post-HCT clinical trial using prophylactic rituximab for the prevention of chronic GVHD (2.2% vs. 11.0%, p=0.011). Clinical disease status was similar between the two groups. Median follow-up for survivors was 4.4 years for Bu1 and 3.2 years for Bu2. Due to the differences in characteristics, the two groups were compared with the adjustment of a propensity score predicting Bu2 to account for measured differences. The day +200 cumulative incidence of grades II-IV acute GVHD (Bu1 17% vs Bu2 8.5%, HR 0.56 [0.22, 1.41], p=0.22) or grades III-IV acute GVHD (Bu1 6.7% vs. Bu2 4.9%) were not different. The 2-year cumulative incidence of chronic GVHD (Bu1 41.5% vs Bu2 28%, HR 0.70 [0.42, 1.17], p=0.09) was not significantly different. 2-year non-relapse mortality (NRM) was similar (Bu1 8.9% vs Bu2 9.8%, HR 0.80 [0.29, 2.21], p=0.67). 2-year progression-free survival (Bu1 40.6% vs Bu2 39.3%, HR 0.82 [0.57, 1.30], p=0.33) and overall survival (Bu1 47.4% vs Bu2 48.8%, HR 0.96 [0.64, 1.44], p=0.85) were also non-significant. Multivariate Cox model with the propensity risk score applied suggest that in a subset of patients with high clinical disease risk and non-adverse cytogenetics, the higher dose busulfan RIC regimen may be of benefit (2-year PFS, HR 0.54 [0.29, 1.03], p=.062). For the majority of patients with MDS/AML undergoing Bu/Flu RIC PBSCT, however, the dose of busulfan (3.2 mg/kg vs 6.4 mg/kg) is not associated with significant differences in overall outcomes.

12

Transplantation Outcomes of 8/8-Matched Unrelated Donors Compared with Matched Siblings and Autologous Transplantation for Acute Myeloid Leukemia with Intermediate Cytogenetics in First Remission

Byung-Sik Cho[1], Seung-Ah Yahng[2], Sung-Eun Lee[2], Ki-Seong Eom[2], Yoo-Jin Kim[2], Hee-Je Kim[3], Seok Lee[4], Chang-Ki Min[2], Seok-Goo Cho[2], Dong-Wook Kim[2], Jong-Wook Lee[5], Jae-Ho Yoon[2], Seung-Hwan Shin[2], Woo-Sung Min[6], Chong Won Park[2]. [1] Hematology, Catholic BMT center, Seoul St. Mary's Hospital, Seoul, South Korea; [2] Catholic BMT center; [3] Catholic Hsct Center, St. Mary's Hospital, Seoul, Republic of Korea; [4] Department of Hematology, The Catholic University of Korea, Seoul, Korea; [5] The Catholic University of Korea, Seoul, South Korea; [6] Catholic Hematopoietic Stem Cell, St. Mary's Hospital Catholic HSCT Center, Seoul, Korea (South)

There have been a few multicenter or registry data assessing the feasibility of unrelated donors (URD) in acute myeloid leukemia (AML) compared to HLA-matched sibling donors (MSD). These studies suggest that MSD and HLA-matched URD have comparable outcomes. However, the small number of patients in first complete remission (CR1) and the lack of high-resolution HLA typing in these studies make it difficult to clearly determine the role of 8/8-matched URD in patients with AML CR1. Furthermore, using 8/8-matched URD is not currently standard practice in patients with AML CR1 having intermediate cytogenetics, particularly those without poor risk features, when MSD are not available. These patients are also candidates for non-allogeneic stem cell transplantation (allo-SCT) therapy, such as autologous peripheral blood stem cell transplantation (auto-PBSCT). In order to clarify the role of 8/8-mateched URD in these patients, transplantation outcomes should be compared with non-allo-SCT therapy as well as MSD.

Between 2002 and 2009, 567 adult patients with AML underwent transplantation from MSD, URD, and autologous sources. According to the risk-adapted treatment strategy, AML CR1 with intermediate cytogenetics received allo-SCT as a post-remission treatment, if MSD or 8/8-matched URD was available. Patients with no available donor received autologous transplantation. To determine the role of 8/8-matched URD on transplantation outcomes in patients with intermediate cytogenetics, we evaluated 288 patients with intermediate cytogenetics who underwent transplantation from autologous sources (n=89) or allogeneic donors (n=199) consisting of 8/8-matched URD (n=54) and MSD (n=145) at CR1.

In multivariate analyses, 8/8-matched URD had comparable 6-year overall survival (OS, P=0.997), disease-free survival (DFS, P=0.951), and relapse (P=0.672) to MSD, whereas 8/8-matched URD had a higher OS (P=0.070) and DFS (P=0.035) with lower relapse (P=0.009) than autologous transplantation. No difference in non-relapse mortality was observed according to donor type. Notably, these equivalent or superior outcomes of 8/8-matched URD compared with MSD or autologous transplantation, respectively, were particularly evident in patients without poor risk features (n=200), such as older age, hyperleukocytosis at diagnosis, and myelodysplasia-related changes, who are not usual candidates for URD transplantation.

In conclusion, this study confirmed the comparable outcomes of 8/8-matched URD with MSD in AML CR1 with intermediate cytogenetics. Additionally, this study strongly suggests that 8/8-matched URD is preferable to auto-PBSCT in AML CR1 with intermediate cytogenetics, when MSD are not available. Finally, our data indicate that 8/8-matched URD are feasible next option in AML CR1 with intermediate cytogenetics, when lacking MSD, even in patients without poor risk features.

13

A 2-Step Approach to Myeloablative Haploidentical Stem Cell Transplantation with Optimized T-Cell Dosing: Early Immune Reconstitution Leads to Better Outcomes

Sameh Gaballa, Onder Alpdogan, Matthew Carabasi, Joanne Filicko, Margaret Kasner, Ubaldo Martinez, John L. Wagner, Mark Weiss, Neal Flomenberg, Dolores Grosso. Department of Medical Oncology, Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA

We developed a 2-step approach to myeloablative haploidentical HSCT in which patients receive a large fixed dose of cyclophosphamide (CY)-tolerized T cells separately frm the HSC infusion in the hopes of accelerating post HSCT immune reconstitution (IR). The uniformity of the T cell dosing facilitates comparison of patients without (low risk) and with (high risk) active malignancy at HSCT to ascertain the impact of disease status at HSCT on IR with fewer confounding effects from conditioning or T cell dosing.